IN THE SPECIFICATION:

Please amend the specification as noted.

1. Please replace existing paragraph **0003** with the following paragraph:

--Tuberculosis (TB) is the primary cause of death due to a single microbial pathogen, accounting for 2 to 3 million deaths and an estimated 8 to 10 million new cases per year worldwide (1). It is estimated that one third of the world's population is infected with *Mycobacterium tuberculosum*. The global epidemic is growing, concomitant with HIV co-infection and the increasing prevalence of drug resistant strains. Genotyping clinical isolates of ~~M.~~ *M tuberculosum* has the potential to significantly impact both clinical practice and public health. Clinically, determining strain relationships can distinguish treatment failure versus potential laboratory cross-contamination, and reactivation of drug-resistant disease versus infection with another strain (24). In the public health arena, determining strain relationships during the course of a tuberculosis outbreak can focus public health resources. However, the most discriminatory ~~M.~~ *M tuberculosum* genotyping method, IS6110 restriction fragment length polymorphism (RFLP) analysis, is time-consuming, technically demanding, and difficult to standardize between laboratories (3). In addition, IS6110 RFLP does not provide sufficient strain discrimination when fewer than six IS6110-hybridizing bands are present. A secondary genotyping method is required in these instances. A number of PCR-based genotyping methods have been developed, but are limited in their ability to reproducibly provide a level of strain discrimination that matches associations defined by traditional epidemiology. In addition, the high degree of coding region sequence conservation between strains of ~~M.~~ *M tuberculosum* virtually excludes the use of more commonly used population genetics methods like multi-locus enzyme electrophoresis, restriction fragment length end labeling analysis, and gene sequencing (12).--

2. Please replace existing paragraph **0013** with the following paragraph:

--In another important aspect of the invention, primer pairs comprising a forward and a reverse primer are presented for amplification of VNTR located in DNA from a *M. tuberculosum* species. Primer pairs suitable for PCR amplification of VNTR, by MLVA or by multiplex, may be selected from the group consisting of SEQ ID NO: 1 and 2, SEQ ID NO: 3 and 4, SEQ ID

NO: 5 and 6, SEQ ID NO: 7 and 8, SEQ ID NO: 9 and 10, SEQ ID NO: 11 and 12, SEQ ID NO: 13 and 14, SEQ ID NO: 15 and 16, and SEQ ID NO: 17 and 18. Certain preferred primer pairs have, in addition, an observable group whereby amplified product may be detected. Such groups may be, for example, a fluorescent group or a radioactive group.--

3. Please replace existing paragraph **0020** with the following paragraph:

--The ultimate utility of VNTR loci lies in their diversity. The present invention discloses the use of marker diversity using both allele number and frequency to sub-type *Mycobacterium ~~tuberculosi~~ tuberculosum* species. VNTR markers that exhibit high diversity values possess great discriminatory capacity for identifying genetically similar strains. Less diverse markers may be applied with greater utility in species identification and the analysis of evolutionary relationships. This demonstrated ability to predict VNTR diversity based upon array size allows the guided selection of marker loci.--

4. Please replace existing paragraph **0058** with the following paragraph:

--The complete genome sequence of the *Mycobacterium tuberculosum H37Rv* strain was downloaded from the Sanger Centre website ~~(www.sanger.ac.uk)~~. Potentially polymorphic repetitive sequences were identified using the DNAstar software program Genequest (Lasergene, Inc Madison, WI). Selection criteria of repetitive sequence were set for nucleotide repeat motifs of more than 8bp within 100 bp proximity of each other. Primers were designed around 84 repetitive sequences identified using the DNAstar software program Primer Select (Lasergene, Inc Madison, WA). Complementary primers were designed around interspersed repeats to minimize risk of mobile DNA targets. Fifteen of these repetitive sequences were found to be polymorphic, i.e., VNTR loci. Nine loci were chosen for use in these analyses (Table. 1).--

5. Please replace existing paragraph **0062** with the following paragraph:

--This example illustrates the amplicon produced during the amplification of VNTR locus Mtb-v1 with primer pairs SEQ ID NO: 1 and SEQ ID NO: 2.

5' Beginning location of VNTR: 55,533. (All accession numbers are according to the H37Rv *M. tuberculosum* sequence done by the Sanger Institute. ~~http://www.sanger.ac.uk/~~)

GGCTCGGGCCTGCCGTCGGACATCTGGAAGGCAACCATGGACGGCGCCTTGAAGGG

CACGTCGAACGAGACTTTCCCCAAACCGACCGAGGTCGGTGGTT

ATGCCGGTGT**GCCGCCGCCGCCGCCGCCGCC**GGAGGTACCACCTTCG**CAG**

ACCGTCATCCAGCCCACGGTCGAAATTGCGCCGGGGATTACCATCCCGATC

GGTCCCCCGACCACCATTACCCTGGCGCCACCGCCCCCGGCCCCGCCCGCTG

CGACTCCCACGCCGCCGCCGTGACCGGCGCGCTGTCCCAAAGCAGCAACATC

TCGCCACTTCCTTTGGCCGCCGATCTGCGGAGCGCCGATAACCGCGATTGCCC

CAGCCGCACCGACGTATTGGG (SEQ ID NO: 19)

FORWARD PRIMER 5' GTCGAACGAGACTTTCCCCAAACCGAC 3'
REVERSE PRIMER 5' GACCGTGGGCTGGATGACGGTCTC 3'

EXAMPLE 2--

6. Please replace existing paragraph **0063** with the following paragraph:

--This example illustrates the amplicon produced during the amplification of VNTR locus Mtb-v3 with primer pairs SEQ ID NO: 3 and SEQ ID NO: 4.

5' Beginning location of VNTR 241,464. (All accession numbers are according to the H37Rv *M. tuberculosum* sequence done by the Sanger Institute. ~~http://www.sanger.ac.uk/~~)

5' GCGAGCCTACCGAAGATCGCGTGCATGCGTTCGGCGTGGACCGCACAGCA

CCTGGAGTTGGCGGCGCCGAGGGCCGAGATGGCAG**GATGACCGATCGTCG**

GGGGCGGGAACTCCCAGGCCGCCGGG**CCGTCGCAAACCCGTCGCAAACC**

CGTCGCAAACCGTAAGGAGTCATCCATGAAGACAGGCACCGCGACGACGCG

GCGCAGGC**TGTTGGCAGTACTGATCGCCCTCGCGTTGC**CGGGGGCCGCCG

TTGCGCTGCTGGCCGAACCATCAGCGACCGGCGCGTCGGACCC,GTGCGCGGC

CAGCGAAGTGGCGAGGACGGTCGGTTCGGTCGCCAAGTCGATGGGCGACT 3' (SEQ ID NO: 20)

FORWARD PRIMER 5' GATGACGGATCGTCGGGGGCGGGAAC 3'
REVERSE PRIMER 5' GCAACGCGAGGGCGATCAGTACTGCCAACA 3'

EXAMPLE 3--

7. Please replace existing paragraph **0064** with the following paragraph:

--This example illustrates the amplicon produced during the amplification of VNTR locus Mtb-v4 with primer pairs SEQ ID NO: 5 and SEQ ID NO: 6.

5' Beginning location of VNTR -241,464. (All accession numbers are according to the H37Rv *M. tuberculosum* sequence done by the Sanger Institute. ~~http://www.sanger.ac.uk/~~)

ATTCAGGCCGCCGAATCCACTACCGATGATGACCACGCGATGGCGCCCGC

CGACGGCCGAGGGTTCACCAGATGAGAGCGTCATGGTCCTCCTTCAGTCTGG

TCGCTGTGGCGCAGCTACACAGTACGACTCCCGTCATGCCAACGGCGTAA

CTTTTT**GTGGGCCTTGTGGGCCTTGTGGGCCTTGTGGGCCTT**TGTCGGGC

CGCCTTCGGATCGGACGCTCGGGATG**GCTGTTGGGCGCTGCGCAATC**CCGC

GCTTCGATCAGGCAGCGTCCGGCAGTGCCATCAATGGCGGCCAGGTACACCT

CTCCGACGGCTCGACATCGCCGGCCCGGCAGTTACCTGCACCATGGCCGGGC

GATGCGGGAGCGGCTGCCGAAGGTCGGGCAGGTGTTTGCTGCCGGGGAAATC

GACTACCACATGTTTCAGACGTTGGTGTATCGCACCGATTTGATCACCGACCC

GCAGGTGTTGGCGCGGGTGGATGCCGAGCTGGCGCTGCGGGTGCGGGGCT (SEQ ID NO: 21)

FORWARD PRIMER 5' GCTGTGGCGCAGCTACACAGTACGACTC 3'
REVERSE PRIMER 5' GATTGCGCAGCGCCCAACAGC 3'

EXAMPLE 4--

8. Please replace existing paragraph **0065** with the following paragraph:

--This example illustrates the amplicon produced during the amplification of VNTR locus Mtb-v5 with primer pairs SEQ ID NO: 7 and SEQ ID NO: 8.

5' Beginning location of VNTR 241,464. (All accession numbers are according to the H37Rv *M. tuberculosum* sequence done by the Sanger Institute. ~~http://www.sanger.ac.uk/~~)

AGCCAGCAGAGCTTCGAGGAAGTGTCGGCGCGCCGAAGGCTACGTGG

ACCAGGCGGTGGAGTTGACCCA**GGAGGCGT[[I']]TGGGTACGGTCGCATCG**CAG

ACCCGCGCGGTCGGTGAGCGTGCCGCCAAGCTGGTCGGCATCGAGCTGCCTA

AGAAGGCTGCTC**CGGCCAAGAAGGCCGCTCCGGCCAAGAAGGCCGCTCC**

GGCCAAGAAGGCGGCGGCCAAGAAGGCGCCCGCGAAGAAGGCGGCGGC

CAAGAAGGTCACCCAGAAGTAGTCGGGCTCCGAATCACCATCGACTCCGA

GTCGCCCACGGGGCGACTCGGAGTCGACGTGTTGGATGCAAACCGCATAGTC

TGAATGCGTGAGCCACCTCGTGGGTACCGTCATGCTGGTATTGCTGGTCGCCG

TCTTGGTGACAGCGGTGTACGCGTTTGTGCATGCTGCGTTGCAGCGGCCCGAT

GCCTATACCGCCGCCGACAA (SEQ ID NO: 22)

FORWARD PRIMER 5' GGAGGCGTTGGGTACGGTCGCATC 3'
REVERSE PRIMER 5' GATTCGGAGCCCGACTACTTCTGGGTGAC 3'

EXAMPLE 5--

9. Please replace existing paragraph **0066** with the following paragraph:

--This example illustrates the amplicon produced during the amplification of VNTR locus Mtb-v6 with primer pairs SEQ ID NO: 9 and SEQ ID NO: 10.

5' Beginning location of VNTR 1,112,923. (All accession numbers are according to the H37Rv *M. tuberculosum* sequence done by the Sanger Institute. ~~http://www.sanger.ac.uk/~~)

GCAGACCGCAGGTGCCGACGAGCCGGACTACTTAGACGTCGATGTGGTC

GAAGAAGACTCGGAGGCGCTTCCGGTGGGGGCTGGCGCTGCGGTCGGCGAGT

CCGCCGACGAGGCCGATGCCGAAGCTGCTGACGGAGTTGCGGGCCACGCC

GACCCGGAGGCCGACCCGGTCG**AATACGAATACGAATACGAATACG**TCGA

GGACACCTGCGGTTTGGAGCTCGAGGAGGACGACCAGGAAGCGCCACCGAC

CGTCGCATCCGGCACGTCACGGCGGCGCCGATTCGACACCAAGACCGCCGCC

GCGGTCAGCGCCCGCAAGTACACCTTCCGCAAACGTGCGTTGATCGTGATGG

CGGTG**ATCCTGGTTGGCTCTGCCGCCGCGG**CCTTCGAGCTGACCCCGGTCG

CGTGGTGGATCTGTGGTAGCGCCACCGGTGTGACGGTGCTCTACCTGGCATAT

TTGCGTCGGCAAACCCGCATCGAGGAGAAGGTGCGTCGGCGGCGGATGCAG

CGGATCGCGCGGGCGCGGCTCGGTGTAGAGAACACCCGTG (SEQ ID NO: 23)

FORWARD PRIMER 5' CGCCGACGAGGCCGATGCCGAAGC 3'
REVERSE PRIMER 5' CCGCGGCGGCAGAGCCAACCAGGAT 3'

EXAMPLE 6

This example illustrates the amplicon produced during the amplification of VNTR locus Mtb-v10. Beginning location of VNTR 2,604,155. (All accession numbers are according to the H37Rv *M. tuberculosum* sequence done by the Sanger Institute. ~~http://www.sanger.ac.uk/~~)

ATCCTTGCAGGTGTTCGGTGGTGACGGTCGTGTTGTCGGCGGCTTCCAGG

CGCAACC**GGAGGCGCCCAGCCCCACAATCAGTGCCAACAGTGCCAACAG**

TGCCAACAGTGCCAGAATCGGGACGGCGCTACGCTGACGACGCACGTCACG

AGCTTAGCGAAAACTGGGAATTTCCCCTACGTTTCATCAACGCC**TCAGGTGT**

CGATCCTAAAGCGCGGGTGCCGCCGGTATTCTTGCCCCAAATCGGTCGGTT

GACACCCGATGCGGTCGGCGAAGCCATCGGCATCGCGGCCGACGACATCCCG

ATGGCGGCACGCTGGATCGGCA.GCCGACCATGCTCGCTCATCGGCCAGCC (SEQ ID NO: 24)

FORWARD PRIMER 5' GGAGGCGCCCAGCCCCACAA 3'
REVERSE PRIMER 5' TCAGGTGTCGATCCTAAAGCGCGGGTG 3'

EXAMPLE 7--

10. Please replace existing paragraph **0068** with the following paragraph:

--This example illustrates the amplicon produced during the amplification of VNTR locus Mtb-v15 with primer pairs SEQ ID NO: 13 and SEQ ID NO: 14. Beginning location of VNTR 3,238,462. (All accession numbers are according to the H37Rv *M. tuberculosum* sequence done by the Sanger Institute. ~~http://www.sanger.ac.uk/~~)

CCGCGCCGATCGGTTCCGTTGATCCGCGCTCCCCGCAGCCGCGCCGTCAGA
TCCGCGGGCCCGGCATCGTGGCGGCGCACAGCGCGGGGGTGGTGCACCCGA
ACCTCGGTGATGGTCCGGCCGGTCACGTGAGCCTGCAAGCC**GCGCCGCACC**
ACCTCGACTTCGGGCAGCTCGGGCAT**CCAGTGATGATCGCAAGCGCGGCG**
AAGCCGGGCGCAGCGGGTCATCACCATCGAACCAGTGATGATCGCAAGC
GCGGCGAAGCCGGGCGCAGCGGGTCATCACCATCGAACCAGTGATGAT
CGCAAGCGCGGCGAAGCCGGGCGCA**GTCCCCCGCAAGCGGGAGGTGCC**
CCCAGGTCATCACCATCGAACCAGTGATCATCGCAAGCGCGGCGAAGCC
GGGCGCAGTCCCCCCCAAGCGGGAGGTGCCCCCAGGTCATCACCATCG
AACCAGTGATGATCGCAAGCGCGGCGAACCCGGCCGCAGTCCCCCGCA
AGCGCGGCAAAGCCGGCGCCCCCAGGTCATCACCATCAATCCA**GTTAGGCG**
GAGGTTTTGCCCGGCATGGCGTTGTCGAGCACTTCCAGGGCTTTCCAAGCG
GCCGCCGCGGCTTTTTGCTCGGCTTCTTTTTTGGACCGGCCCACTCCTGAAC (SEQ ID NO: 25)

FORWARD PRIMER 5' GCGCCGCACCACCTCGACTT 3'
REVERSE PRIMER 5' GTTAGGCGGAGGTTTTGCCCGG 3'

EXAMPLE 8--

11. Please replace existing paragraph **0069** with the following paragraph:

--This example illustrates the amplicon produced during the amplification of VNTR locus Mtb-v18 with primer pairs SEQ ID NO 15 and SEQ ID NO 16.

5' Beginning location of VNTR 4,227,024. (All accession numbers are according to the H37Rv *M. tuberculosum* sequence done by the Sanger Institute. ~~http://www.sanger.ac.uk/)~~

CGGGCTATCACCGGTTCATCTTCTGGGCCTATGGCCGCAACGGGGAGAGCG

ATCCTCGGGTACTCGAGGCCATCCAAGTCCTCCGTATCCGCTATATCCTGACC

AGCACTCCGACGGTGCGGGGGTTTGCCGTGCCGGACGGACTAGTGTCGTTAG

AGACATCGAGGTCGTGGGCGAAGATCTACG**ACAACGGCGAGGCCCGAATC**

TACGAATGGCGCGGCACTGCCGCAGCAACACACTCCTAGAAGGTGCGTAAG

AGGATGGTGATTGGATTGAGTACCGGCAGCGACGACGACGACGTCGAGGTCA

TCGGCGGCGTCGACCCGCGGCTGATAGCGGTGCAGGAGAACGACTCCGACG

AGTCGTCGCTGACCGACCTGGTCGAGCAGCCCGCCAAGGTGATGCGCATCGG

`CACCATGATCAAGCAACTGCTCGAGGAGGTTCGCGCCGCCCCACTCGACGAA

GCCAGCCGCAATCGGCTACGCGA**TATCCACGCCACCAGCATCCGCG**AACTC

GAAGATGGTCTGGCCCCGGAACTGCGCGAGGAGCTCGACCGGCTTACCCTGC

CGTTCAACGAGGACGCCGTGCCCTCGGACGCCGAGTTGCGCATTGCCCAGGC

ACAGCTGGTCGGCTGGCTGGAAGGGCTGTTCCACGGCATCCAAA (SEQ ID NO: 26)

FORWARD PRIMER 5' ACAACGGCGAGGCCCGAATCTACGAA 3'
REVERSE PRIMER 5' ATAGGTGCGGTGGTCGTAGGCGC 3'

EXAMPLE 9--

12. Please replace existing paragraph **0070** with the following paragraph:

This example illustrates the amplicon produced during the amplification of VNTR locus Mtb-v20 with primer pairs SEQ ID NO 17 and SEQ ID NO 18. Beginning location of VNTR 23,693. (All accession numbers are according to the H37Rv *M. tuberculosum* sequence done by the Sanger Institute. ~~http://www.sanger.ac.uk/~~)

AGCGTATCCCGGGACCCGCGGGGATTCGGTGTAGCGGGTGTAGTCAGCGCC

GCCGCCATAGTCTTGCCGGCCGTATGTCGTGGCGCCTTGCTGGTAGCCCTGGT

CGTAACCGCCTTGGTCGGGGTAAGCCGGTCGTTGCTCGGGCGGG**CCCGGAG**

GGCCAGAGGGCACATAGCTGCCCTCCTCGTGGCGAGCCGGGCCACGCCCGT

ACTCCCCGTACCCGCCGTAGCCGGGCTGGCCGCCACCGGGTGAAGGGCCGTA

GCCGCCGCTTTGGCGATAGCCCTGGTCGTAGCCGGGAGCGCCGTAGCCGGCA

GCCGGGCCGGGAGAAACAGGAGGGCGTTGCTCGTAGGGCGGCGGATAGCCC

CCCTGCCCTTGGTCGGGGTAGCCTCGACCCTGGTCCTGGTACCCGCGCTGGTC

GGGGTAG**CCGCGTTGCTCGGGGTAACCGCGTTGCTCGGGGTAACCG**CCC

TGGTCGGGGTACCCGATTTGCTCGGGGTAGTCGCCCTGGTCCGGGTGGCGCG

GGCGTGGGTAGCCCGGCTGGGGCGGGTAGCCGCCCGTCTCGGGTGGATACCC

CCCGCGGGGGTCAGATCCGCCTTGCGGATCCGGGCCACCACGCGGATCCTCT

TGCGGACGCGCATAGCGGTCGTCGTAATACTCGTCGGGACGCCCCTGCCCCT

GACCGCCACGGTAGCTCGAAT**TGTCACTCATTGGTGCTACTCCTGGTTCTG**

CGCCAAACGCGTGGTTTGATTGTGGCCGGGCGCAATCGATGACCGGCGG (SEQ ID NO: 27)

FORWARD PRIMER 5' CCCGGAGGGCCAGAGGGCACATAGC 3'
REVERSE PRIMER 5' GTCACTCATTGGTGCTACTCCTGGTTCTGCGCCA 3'--

13. Please replace the existing **Sequence Listing** with the Sequence Listing appended to the end of this Response.

14. Please add **pages 28 and 29** to the specification (appended to the end of this response).

15. Please replace the existing **Abstract** with the following Abstract:

(On separate sheet in accordance with 37 C.F.R. 1.72; see next page).